In the Claims

Applicants submit herewith a marked-up version of the claims. Entry of the amendments is requested. Please amend claims 1, 10, 11, 18, and 33 as shown on the marked up versions of the claims. Please add new claims 38 and 39 as shown on the marked-up version of the claims.

The submitted marked-up versions of the claims follows standard amendment rules, wherein added text has been underlined and deleted text has been bracketed. The status of each claim is additionally provided.

Remarks to Amended Claims

Claim 1 has been amended to make to additions and deletions to the claim. First, the preamble of claim 1 has been amended to indicate "A method of measuring changes of concentration of an analyte in the body of a patient." Support for claiming a method of measuring changes of the concentration of an analyte in the body of a patient is one of the central aspects of Applicants disclosure (see summary of the invention on pages 1-4, and throughout the specification). The second change that was made to claim 1 inserts that the aspect that the detected change in concentration of the analyte is a function of the change of the detected energy. This occurs, as indicated by the claim, by the fact that the energy is captured and transmitted by said second dye in response to the emitted energy at said first wavelength. The addition of the second amendment is to tie together the elements of the claim so that the measured energy changes are related to the resultant concentration changes of the analyte. Third, Claim 1 has been broadened to remove reference to solely measurements of concentration of troponin, and now includes any analyte system. Fourth, the claim has been amended to require that at least the light emitter or light detector is also implanted in the body. These implantable elements are discussed in the specification at paragraphs [0032] and [0033] in discussion of Figure 2, wherein it is shown an implantable light emitter and light detector.

Claim 10 as been amended to focus the claim on a particular attribute of analyte sample as given in the first part of the claim. As amended, claim 10

indicates the analyte comprises at least a D-dimer. Rest of the language of previous claim 10 has been removed and submitted as new claim 38.

Claim 11 has been amended to add to the preamble that the system is for measuring changes of concentration of an analyte in the body of a patient. Support for claiming a method of measuring changes of the concentration of an analyte in the body of a patient is one of the central aspects of Applicants disclosure (see summary of the invention on pages 1-4, and throughout the specification). Second, Claim 11 has been broadened to remove reference to solely measurements of concentration of troponin, and now includes any analyte system. Third, the claim has been amended to require that at least the light emitter or light detector is also implanted in the body. These implantable elements are discussed in the specification at paragraphs [0032] and [0033] in discussion of Figure 2, wherein it is shown an implantable light emitter and light detector.

Claim 18 was previously presented as an amendment, but was not listed to be entered. Applicant's apologize for this oversight and ask for entry of the amendment to Claim 18 if it was not previously entered. The amendments to the claim, as previously indicated, help clarify the language of the claim.

Claim 33 has been amended to require that at least the light emitter or light detector is also implanted in the body. This is discussed in the specification at paragraphs [0032] and [0033] in discussion of Figure 2, wherein it is shown an implantable light emitter and light detector.

Claim 38 is new. Claim 38 is directed to indicate that the detected change relates to a change in the concentration of the analyte of a patient having occurred after an ischemic stroke or viral infection, or after administration of one of the group consisting of medication, insulin, an illegal drug, a biological toxin, and a biological warfare agent. The claim language of Claim 38 was originally found in Claim 1 but now stands a separate dependent claim.

Claim 39 is new. Claim 39 specifically defined as an dependent claim of claim 1 the aspect that the detected analyte is troponin. Support for the analyte is

troponin is found in the specification at paragraphs [0011], [0027], Figure 1, and numerous other places in the specification.

Applicants' Response

Applicants respond below to each section of recent Examination by including (1) a restatement of the rejection/objection in single spaced type, followed by (2) Applicant's response in double space type.

Claim Rejections - 35 USC § 112

Claim 10 was rejected under 35 USC § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner indicated it was unclear how the limitation of claim 10 can be met, as independent claim 1 sets forth that the analyte detector is for troponin, and it is unclear how the detected analyte can be both troponin and one of the analytes set forth in claim10.

Applicants have amended claim 10 to break it apart into two independent claims. Claim 10, as amended, is directed to that aspect of the original claim that indicates the analyte comprises a D-dimer. Rest of the language of previous claim 10 has been submitted as new claim 38, wherein that claim is directed to indicate that the detected change relates to a change in the concentration of the analyte of a patient having occurred after an ischemic stroke or viral infection, or after administration of one of the group consisting of medication, insulin, an illegal drug, a biological toxin, and a biological warfare agent. All these indications relating to the source of the sample being tested could be found in claim 10 as originally presented but in a more readable form.

In view of the submitted amendments, Applicants respectfully request the present rejection of claim 10 under 35 USC § 112, second paragraph, be removed.

Claim Rejections - 35 USC § 101

Claims 1, 2, 4 - 10, and 18 were rejected under 35 USC § 101 because the claimed invention was indicated to be directed to non-statutory subject matter. With regard to claims 1, 2, and 4 - 10, the Examiner has indicated it appears to be directed to processing data to determine physiological information rather than a practical application involving the physiological information. As such the Examiner has further indicated that the claim does not result in a physical transformation nor does it appear to provide a useful, concrete and tangible result. Specifically, it does not appear to produce a tangible result because merely detecting a change in a concentration is nothing more than a computation within a processor. The claimed invention fails to use or make available for use the result of the detecting to enable its functionality and usefulness to be realized. Additionally, the asserted practical application in the specification is for generating an alarm or controlling a therapy device based upon the results. The practical application is not explicitly recited in the claims nor does it flow inherently there from. Therefore, claim 1 appears to be non-statutory. In addition, dependent claims 2, and 4 - 10, while reciting further limitations, fail to explicitly or inherently recite the practical application.

With regard to claim 18, the claim improperly includes a living subject as part of the claimed subject matter by reciting "are implanted in the body". The claim should be amended to recite "are adapted to be implanted in the body" to avoid this problem.

The Examiner has indicated that the claimed invention fails to use or make available for use the result of the detecting to enable its functionality and usefulness to be realized.

Applicants have amended claim 1 to indicate that the detected change in concentration of the analyte (the result) is a function of the change of detected energy captured and transmitted by said second dye in response to the emitted energy emitted at said first wavelength (the measurement). Applicants submit that the amended claim now provides within the claim, the means to measure the changes of an analyte. The ability to measure changes in an analyte is known to be useful.

In view of the submitted amendments, Applicants respectfully request the present rejection of claims 1, 2, 4-10, and 18 under 35 USC § 101 be removed.

Claim Rejections - 35 USC § 103

Claims 1 - 8, 10, 11, 13 - 16, 19 - 21, and 33 - 37 were rejected under 35 USC 103(a) as being unpatentable over Chick et al. (USPN 6,040,194 - previously cited) in view of Wicks et al. Chick et al. was cited for teaching a method and arrangement for detecting an analyte in the human body comprising placing an analyte detector with two fluorescent dyes within the body, illuminating the detector, and measuring the analyte concentration based upon the ratio of energy emitted by the two dyes as a result of fluorescent resonant energy transfer (FRET) between them (col. 2, line 31 - col. 6, line 44) . Further, the Examiner has indicated that Chick et al. teaches a drug delivery system in communication with the analyte detector may be implanted in the body such that a feedback loop is established wherein a prescribed amount of drug is released when the measured analyte concentration exceeds a certain threshold (col. 6, lines 1-5) . The illuminating energy is visible light at a wavelength of 472 nm (col. 11,lines 36-47) and the analyte measured may be a protein in the blood (the level of which may vary under certain physiological states) or an antigen or a narcotic such as cocaine or heroin (col. 5, lines 15-50) . Thus, the Examiner has concluded that Chick et al. teach all of the features of the invention except that the sensed protein is troponin. However, the Examiner has cited Wicks et al. for teaching that troponin I is a protein that is a marker for cardiac damage (column 1, lines 24 - 41). Therefore, the Examiner has concluded that it would have been obvious to one of ordinary skill in the art at the time of the invention to implement Chick et al. with sensitivity for troponin, since Chick et al. teach that their method and arrangement are suitable for detecting proteins in the blood that are indicative of physiological states and Wicks et al. teach that troponin I is a blood protein that is a marker for cardiac damage.

Although, Chick et al. teaches a FRET detector system, and Wicks suggests that troponin 1 is a protein marker for cardiac change, no where in either reference, or in combination, is there a teaching or suggestion that one can make an analyte FRET detector wherein in addition to the analyte detector, the light emitter or the light detector is also implanted. Further, neither Chick et al. nor Wicks suggest the merits of such a system over other analytical approaches.

First, in reference to Figure 2 and Figure 3, Applicants show two types of analytical systems. Figure 3 shows the FRET device wherein only the analyte detector is implanted and the light emitter and the light detector are externally located. This is comparable to the FRET systems described by Chick et al. (more discussion later). Figure 4 shows a FRET device wherein the analyte detector, light emitter and light detector are implanted.

Chick et al. mentions in the specification that it is an implantable system; however, the only implantable system described by Chick et al. is where the analyte detector is implanted. In Chick et al. no reference is made of implanting the light emitting source or the light detecting source. The only reference in Chick et al. appears in Example 6, where at column 17, lines 39-43, it is indicated that the Pan-69 fiber (the analyte detector) is implanted. However, it specifically goes on to indicate the mouse was placed in a fluorimeter so that the implanted fiber was

externally illuminated, and that the florescence was externally detected. Here, neither the light emitter nor the light detector is implanted. Further, there is no teaching or suggestion to do so or any suggestion that this is even desirable. The only implantable system described by Chick et al. is where the analyte detector is implanted, but both the light emitter and the light detector are external.

In view of the submitted amendments and arguments, Applicants respectfully request the present rejection of Claims 1 - 8, 10, 11, 13 - 16, 19 - 21, and 33 - 37 under 35 USC § 103, be removed.

Claim 9 was rejected under 35 USC § 103(a) as being unpatentable over Chick et al. and Wicks et al. as applied to claim 1 above, and further in view of Khaw et al. The combination of Chick et al. and Wicks et al. was cited for teaching all of the features of the claimed invention except that the analyte is cardiac troponin-T antigen. However, Khaw et al. was cited by the Examiner for teaching that troponin I and T are alternate equivalents for sensing heart attack related events (paragraphs [0002] and [0011]). Chick et al. was cited by the Examiner for teaching that the antigen is used to detect a protein (column 9, line 59 - column 12). In view of the cited references the Examiner has indicated that it would therefore have been obvious to one of ordinary skill in the art at the time of the invention to modify the combination of Chick et al. and Wicks et al. to sense troponin T, since Khaw et al. teaches that this is an alternate equivalent expedient and it has generally been held to be within the skill level of the art to substitute alternate equivalent expedients.

In line with the previous reasoning, even though Chick et al. teaches a FRET detector system, and Wicks suggests that troponin 1 is a useful cardiac marker, and Khaw teaches that troponin I and troponin T are alternate equivalents as a protein marker for cardiac change, no where is there a teaching or suggestion that one can make an analyte FRET detector wherein in addition to the analyte detector, either at least the light emitter or light detector is also implanted.

Chick's implanted system only has an implanted analyte detector. There is no teaching or suggestion how to make or use a system wherein at least either the light emitter or light detector is implanted. In view of the lack of teaching in Chick et al. that describes an operable system wherein the light detector and/or light emitter are implanted, Applicants respectfully request the present rejection to claim 9 be removed.

Claim 12 was rejected under 35 USC § 103(a) as being unpatentable over Chick et al. and Wicks et al. as applied to claim 11 above, and further in view of Kwon (previously cited). The Examiner has indicated that the combination of references teaches all of the features of the claimed invention except for the particularly claimed fluorescent dyes. Kwon was cited for teaching monitoring analyte concentrations in the body using FRET, wherein one of the dyes which may be used is tetramethylrhodamine isothiocyanate. Based on the combination of references the Examiner has concluded that it would have been obvious to one having ordinary skill in the art at the time the invention was made to use with the FRET system disclosed by the combination with the fluorescent dye tetramethylrhodamine isothiocyanate, since Kwon teaches that this dye allows for effective FRET analyte concentration measurements.

As previously indicated, even though Chick et al. teaches a FRET detector system, and Wicks suggests that troponin 1 is a useful cardiac marker, and the fact that Kwon teaches analyte concentrations in the body can be determined by FRET technology, no where in these references, or in combination, is there a teaching or suggestion that one can make an implantable FRET detector wherein in addition to the implanted analyte detector, either at least the light emitter or light detector is also implanted.

As in Chick et al., Kwon only shows a system where the analyte detector is implanted (referred to in Kwon as the "reporter system"). Both Chick et al. and Kwon describe glucose reporter systems that have implanted the analyte detector. Kwon discusses injectable reporter systems (i.e., the analyte detector), whereas the system of Chick et al. surgically implants a needle like detector apparatus under the skin. Like Chick et al., Kwon uses an external light emitter and detector. Kwon on page 2, paragraph [0012], indicates that the sensing apparatus is placed in contact with the target tissue (i.e. not implanted). The Examiner should note that Kwon's sensing apparatus serves as both as the emitting and detecting apparatus.

In view of Applicants claims specifically recite that at least the light emitter or light detector are implanted, and this distinction is neither taught or suggested by Chick et al., Wicks et al., or Kwon, individually or collectively, Applicants, respectfully request the present rejection of Claim 11 over Chick et al. and Wicks et al. in view of Kwon be removed.

Claim 17 is rejected under 35 USC § 103(a) as being unpatentable over Chick et al. and Wicks et al. as applied to claim 11 above, and further in view of Rao et al. (previously cited) . The Examiner argues that the combination of references teaches all of the features of the claimed invention except that there is an alert module. Rao et al. teach an alternate FRET system that includes an alert module notify a subject of changes in concentration (see Figure 9 and the description thereof). Therefore the Examiner argues it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the combination to include an alert module, as taught by Rao et al., since this allows a subject to be notified of changing concentrations.

Although, Chick et al. teaches a FRET detector system, and Wicks suggests that troponin 1 is a protein marker for cardiac change, and Rao et al. teach an alternate FRET system that includes an alert module that can notify a subject of changes in concentration, no where in these references, or in combination, is there a teaching or suggestion that one can make a FRET detector that has an implanted light emitter or light detector.

Applicants have previously discussed the arguments as to why Chick et al. and Wicks et al. are insufficient to show the present invention is obvious. The addition of Rao that teaches an alert module does not help overcome the problem that the previous references do not teach or suggest that either the light emitter or detector is implantable. Knowing that the system can have an alert module to notify the subject adds nothing to fill this void.

In view of Applicants claims that specifically recite that at least the light emitter or light detector are implanted, and this distinction is neither taught or suggested by Chick et al., Wicks et al., or Kwon, individually or collectively, Applicants, respectfully request the present rejection of Claim 11 over Chick et al. and Wicks et al. in view of Rao be removed.

Claim 18 was rejected under 35 USC § 103(a) as being unpatentable over Chick et al. and Wicks et al. as applied to claim 11 above, and further in view of Van Antwerp et al. The Examiner argues that the combination of references teaches an implantable sensor with transdermal determination of analyte concentrations (column 6, lines 6 - 34 ; column 16, line 23 - column 17, line 32). Van Antwerp et al. (Figure 6 and the description thereof) was cited by the Examiner for teaching an alternate arrangement that includes a completely implantable emitter, detector, and sensing elements. Therefore, the Examiner concludes it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the combination to use a completely implantable arrangement, as taught by Van Antwerp et al., since this is merely an alternate equivalent expedient.

Although, Chick et al. teaches a FRET detector system, and Wicks suggests that troponin 1 is a protein marker for cardiac change, no where in either reference, or in combination, is there a teaching or suggestion that one can make a FRET detector having either an implanted light emitter or light detector. Van Antwerp et al. teaches that you can implant the emitter, sensing elements in a fluorescence quenching system. Van Antwerp et al. does not teach the claimed FRET system, and therefore does not overcome the fundamental questions as to whether one could successfully make an implantable FRET detection system containing an implanted light emitter or detector.

The fluorescence quenching system of Van Antwerp et al. is illustrated in Figure 10. In essence, binding of glucose to the borante region of the fluorescent moiety causes a quenching effect that can be measured. This differs from the FRET based energy transfer system claimed wherein upon binding of the analyte it causes a change in the energy transfer between two matched dye compounds.

Based upon Applicants arguments and amendments to the claims that Van Antwerp et al. is describing a non-FRET based implanted system, and Applicants earlier arguments that Chick et al. in view of Wicks et al. does not teach such an implanted system, Applicants respectively request the present rejection over these references be removed.